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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,485	10/17/2001	Brenda F. Baker	RTS-0139	5056

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,485	BAKER ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-10 and 12-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-05-2005 has been entered.

2. The amendment to the claims filed on 4-05-2005 does not comply with the requirements of 37 CFR 1.121(c) because claim 11 recites the wrong status identifier. In the amendment filed 10-27-04 Applicants cancelled claim 11, the current amendment does not reflect the cancellation of claim 11. The current amendment recites claim 11 as (Original), and sets forth the original text of the claim. If Applicants intended to reinstate the claim, the claim may only be reinstated by adding the claim as a "new" claim with a new claim number.

Amendments to the claims filed on or after July 30, 2003 must comply with 37 CFR 1.121(c). Therefore, claim 11 will not be examined in the instant Office Action, because the claim was cancelled in the amendment filed 10-27-04.

Response to Arguments

3. Applicant's arguments with respect to claims 1-2, 4-10 and 12-14 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Eisen et al.

The instant claims are drawn to a compound 8 to 80 nucleobases in length targeted to nucleobases 381 through 502, or nucleobases 629 through 713 of a nucleic acid molecule encoding matrix metalloproteinase 1 (SEQ ID NO: 3), wherein said compound specifically hybridizes with said nucleic acid encoding matrix metalloproteinase 1.

Eisen et al. discloses an oligonucleotide of 17 nucleobases, wherein the complement of this sequence is 100% identical to nucleobases 418 through 434 of SEQ ID NO: 3.

The complement of the oligonucleotide disclosed by Eisen et al. exhibits 100% local similarity between nucleobases 381 through 502 of a coding region of a nucleic acid molecule encoding matrix metalloproteinase 1 SEQ ID NO: 3 of the instant invention. Given this high degree of complementarity, the antisense oligonucleotide disclosed by Eisen et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" with a nucleic acid molecule encoding matrix metalloproteinase 1 as defined in the instant specification at page 8, line 31 through page 9, line 13. Accordingly, the oligonucleotide disclosed by Eisen et al. would specifically hybridize to bases 381 through 502 of SEQ ID NO: 3 as claimed.

The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the oligonucleotide disclosed by Eisen et al. would or would not have the additional functional limitation of "inhibiting expression" of matrix metalloproteinase 1 under general any assay conditions.

Therefore, absent evidence to the contrary, Eisen et al. is considered to anticipate instant claims 1-2.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-2, 4-6, 8, 10, 12, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Kurreck et al. (US 2004/0002473 A1; 102(e) priority date of August 31, 2001, the filing date of the instant application is October 17, 2001).

8. The instant claims are drawn to a compound 8 to 80 nucleobases in length targeted to nucleobases 381 through 502, or nucleobases 629 through 713 of a nucleic acid molecule encoding matrix metalloproteinase 1 (SEQ ID NO: 3), wherein said compound specifically hybridizes with said nucleic acid encoding matrix metalloproteinase 1.

9. Kurreck et al. discloses an antisense oligonucleotide of 17 nucleobases in length (see SEQ ID NO: 8 of Kurreck et al.), wherein the complement of this sequence is 88.2% identical to nucleobases 436-452 of SEQ ID NO: 3 of the instant application.

The complement of the oligonucleotide disclosed by Kurreck et al. exhibits 88.2% local similarity between nucleobases 381 through 502 of a coding region of a nucleic acid molecule encoding matrix metalloproteinase 1 SEQ ID NO: 3 of the instant invention. Given this high degree of complementarity, the antisense oligonucleotide disclosed by Kurreck et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" with a nucleic acid molecule encoding matrix metalloproteinase 1 as defined in the instant specification at page 8, line 31 through page 9, line 13. Accordingly, the oligonucleotide

disclosed by Kurreck et al. would specifically hybridize to bases 381 through 502 of SEQ ID NO: 3 as claimed.

The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the oligonucleotide disclosed by Kurreck et al. would or would not have the additional functional limitation of "inhibiting expression" of matrix metalloproteinase 1 under general any assay conditions.

The antisense oligonucleotides of Kurreck et al. preferably comprises at least one modified or unmodified ribose, at least one modified or unmodified phosphodiester bond (particularly phosphorothioate linkages) and/or at least one modified or unmodified base (see

paragraphs [0015]-[0016]). The invention of Kurreck et al. also contemplates chimeric oligonucleotides, comprising one or more nucleotides that are "locked nucleic acids" (LNAs) or wherein all of the nucleotides are phosphorothioate and wherein two or more of the nucleotides are LNAs (see paragraph [0016]).

The disclosure of Kurreck et al. also contemplates compositions comprising the antisense oligonucleotides of the invention. The compositions of Kurreck et al. may be packaged in a liposome (see [0039]). In particular, Kurreck et al. describes pharmaceutical preparations in the form of solutions for injection, semi-solid forms, tablets, coated tablets, capsules, granules, drops, and syrups are suitable for oral administration. Furthermore, Kurreck et al. teach that preparations comprising solutions, suspensions, easily reconstitutible dried preparations and sprays are suitable for parenteral, topical and inhalatory administration (see paragraph [0041]).

Therefore, absent evidence to the contrary, Kurreck et al. anticipate claims 1-2, 4-6, 8, 10, 12, and 14.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-2, 4-10, and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurreck et al. in view of Monia et al. (US 6,114,517, Monia et al. was cited in the prior Office Action).

The discussion of Kurreck et al. as set forth above is incorporated here. However, Kurreck et al. does not disclose antisense oligonucleotides comprising a 2'-O-methoxyethyl sugar modification, or a 5-methyl cytosine nucleobases modification. Additionally, Kurreck et al. does not specifically teach pharmaceutical compositions further comprising a colloidal dispersion system.

Monia et al. teach the design of antisense oligonucleotides comprising various modifications, including phosphorothioate modified internucleoside linkages (col. 8, line 41-43), 2'-O-methoxyethyl sugar modifications (col. 10, line5), and a 5-methylcytosine modified nucleobase (col. 10, line 31-32). The modified or substituted oligonucleotides of Monia et al. are preferred over native (unmodified or unsubstituted) forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced binding to target and increased stability in the presence of nucleases (col. 8, lines 2-6). Additionally, Monia et al. teach the use compositions comprising antisense oligonucleotides and a pharmaceutically acceptable carrier or diluent, and further comprising a colloidal dispersion system in order to enhance the stability of oligonucleotides introduced into cells and to target oligonucleotides to a particular tissue or cell (col. 15, lines 19-41).

It would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of Kurreck et al. and Monia et al. to design the compounds and compositions according to the present invention. One of ordinary skill in the art would have been motivated to modify the antisense compounds of Kurreck et al. to comprise 2'-O-methoxyethyl sugar modifications, or a 5-methylcytosine modified nucleobases, because according to Monia et al. antisense oligonucleotides comprising these modifications would enhance the cellular

properties of antisense oligonucleotides as compared to unmodified antisense compounds. Moreover, one of ordinary skill in the art would have been motivated to design compositions comprising the antisense compounds according to the present invention and a pharmaceutically acceptable carrier or diluent, and further comprising a colloidal dispersion system because Monia et al. teach that compositions designed according to this manner would enhance the stability of oligonucleotides introduced into cells and would help to target oligonucleotides to a particular tissue or cell.

Therefore, the invention as a whole is *prima facie* obvious over Kurreck et al. in view of Monia et al.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1635

JLE